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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LIU, SAMUEL W	
ART UNIT	PAPER NUMBER
1653	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/782,953	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-101* is/are pending in the application.

4a) Of the above claim(s) *1-58 and 63-101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 7/12/01 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The response filed 2 December 2002 as to request for extension of time of one-month has been entered. Applicant's election without traverse of Group XIV, claims 59-70 (Paper No. 13) filed on December 2, 2001 is acknowledged. Yet, in the paper, applicant dose not elect a promoter that is required by the restriction requirement sent 2 October 2000. On a telephone conversation with Steven Highlander on January 30, 2003, peptide was elected from claim 62 (see the attached interview summary). Since claims 63-70 are drawn to a process involving non-peptide agonist, claims 63-70 are drawn to non-elcted invention. Affirmation of this election must be made by applicants in replying to this Office action. Thus, claims 1-58 and 63-101 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Therefore, elected claims 59-62 together with the elected promoter are examined in this Office action. .

Specification/Claim/ Objections

The disclosure is objected to because of the following informalities:

(1) In page 1, line 8, the term "MCIPs" should be spelled out in full at the first instance of use. See also page 1, line 15, "NFAT", line 21, "AP1", line 26, "cMAF", line 27, "GATA", and line 28, "MEF2"; page 5, line 24, "RT-PCR, and "ELISA"; page 9, line 30, "NFATc"; page 10, line 30, "GST"; page 13, line 5, MHC"; page 24, line 19, "PEG"; page 25, line 1, "HPLC" and line 8, "SDS-PAGE"; page 37, line 20, "HSV"; page 44, lines 3-4, "DHFR" and "GPT"; page 59, lines 24-25, "RFLP", "PCR" and "SSCP"; and page 89, line 12, "SP".

(2) In page 28, line 3, "SEQ ID:5" should be changed to "SED ID NO:5.

(3) In page 28, line 2, "MCIP2" should be changed to "MCIP1".

(4) In page 28, line 4, the recitation "SEQ ID NO:5 and 16" is confusing because SEQ ID NO: 16 is not a polynucleotide but a polypeptide sequence. See also "SEQ ID NO:3" recited at page 28, line 3, which is a protein not a DNA sequence. The similar corrections must be made throughout entire specification, *e.g.*, at page 31, line 8, polynucleotide sequences SEQ ID NOs: 3, 7, 9 and 16 are recited as polynucleotides.

(5) In page 29, line 19, "7.9" should be changed to "7, 9". In page 30, line 8, "16also" should be changed to "16 also".

(6) In page 83, line 15, "(NFAT)" should be deleted.

Appropriate correction is required.

Drawing

The drawings filed 13 February 2001 are objected to under 37 CFR 1.84(h)(5) because Figure 9 shows modified forms of construction in the same view. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Applicant is required to submit a proposed drawing correction in reply to this Office action. However, formal correction of the noted defect may be deferred until after the examiner has considered the proposed drawing correction. Failure to timely submit the proposed drawing correction will result in the abandonment of the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 59-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 59 recites "modulation"; the recitation is not clear as to whether or not the modulation refers to up- or down-regulation. The dependent claims are also rejected. Also, claim 59 is indefinite because the claim is vague as to the subject matter to which the claim is directed. Applicant elects agonist as a peptide. Yet, it is not clear how the peptide is administered, *i.e.*, transferred, into the muscle cell. Is the administration carried out by a direct mean, *i.e.*, protein transfection, or by an indirect mean, *i.e.*, expression of the transferred gene that encodes the said peptide?

Claim 60 recites the limitation "a mammal". There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of the method of promoting muscle cell growth via controlling activity of a promoter located up-stream of a transferred gene encoding MCIP protein in a subject. Applicant is not in possession of a method of modulating muscle cell growth comprising administering a peptide agonist stimulating the muscle cell growth thereof. There is insufficient written description about what peptide or protein factors involve in this regards and how to administer the peptide agonist to the subject. One of skill in the art would reasonably conclude that the disclosure insufficiently provides a representative number of species to describe the genus that is "peptide". Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claims 59-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modulating MCIP protein expression at transcriptional level by controlling promoter activity of the expression vector containing a gene encoding MCIP in mammalian cells or mammals, does not reasonably provide enablement for a method of modulating muscle cell growth comprising administering a

peptide or an agonist thereof to the subject, which is the subject matter of the current application. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The application disclosure and claims have been compared per the factors indicated in the decision *in re* Wands 8 USPQ2d 1400, 1400 (Fed. Cir. 1998). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but not limited to: 1) the nature of the invention; 2) the breath of the claims; 3) the predictability or unpredictability of the art; 4) the amount of direction or guidance presented; 5) the presence or absence of working examples; 6) the quantity of experimentation necessary; 7) the relative skill of those skilled in the art.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

(1) The scope of the claims/The nature of the invention:

Claims 59-62 set forth a method of administering a peptide to muscle cell. The specification does not reasonably provide guidance and working examples as to what peptide is used in the method and how to administer the peptide molecule to the subject for modulating muscle cell growth. Therefore, the scope of claims is outside the bounds of the enablement and would have resulted in the necessity of undue experimentation.

(2) The unpredictability of the art:

Applicant elects peptide that is a genus encompassing numerous proteinous factors or fragments for the claimed method. Thus, the genus is highly variable. The current disclosure does not describe representative species from the genus. Prediction of outcome of the use the peptide(s) is therefore highly variable.

(3) The state of the prior art:

The general knowledge and level of skilled in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe common attribute and characteristics that identify any pharmaceutical agent qualified for cardiac therapy. As stated above, because the genus is highly variant, the specification needs to provide sufficient guidance to be considered enabling.

On the other aspect, since the disclosure sets forth that the muscle cell to be administered is located in a mammal (see claim 60). The skilled artisan would have not known what and how a peptide agonist is administered to target muscle cells without degradation or cytotoxicity. Thus, the outcome of using peptide species for the MCIP expression modulation is unpredictable as well.

(4) The quantity of experimentation necessary:

In the absence of working examples with regard to the genus stated above, unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention. The quantity of experimentation would be large and unpredictable. One skilled in the art would be required to carry out an undue experimentation for screening and

characterizing the peptide agonist(s) that up-regulates muscle cell growth *via* controlling MCIP expression.

(5) The relative skill of those in the art:

The general knowledge and level of skill in the art do not supplement the omitted description with respect to a massive number of variant sequences of peptide. In view of the preceding factors (1-4), the level of skill in this art is high and requires at least a cell biologist or a physician with several years of experience in molecular biology as well as knowledge in cardiology and pharmacology; yet, even with a level of skill in the art as those mentioned in precedence, predictability of the results is still highly variable. An unduly level of skill is needed for the skilled artisan in order to identify suitable peptide agonist for the MCIP expression-governed muscle cell growth, and treatment a cardiac disease state thereof.

In consideration of each of factors stated above, absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 59-62 are rejected under 35 U.S.C. 102 (b) as being anticipated by Miyazaki, T. *et al.* (*J. Biol. Chem.* (1996) 271, 14567-14571).

Miyazaki, T. *et al.* teach that ZAKI-4 protein that is a member of a human family of calcineurin binding protein is expressed in skeletal muscle cell (see the data shown in Figure 6, and abstract) and that ZAKI-4 protein expression is regulated by thyroid hormone through thyroid hormone receptor (see the first paragraph of introduction at page 14567) and "Discussion" section). Also, Miyazaki, T. *et al.* teach a method of transferring thyroid hormone responsive factor, *e.g.*, thyroid hormone receptor, into mammalian cells by gene cloning (see the second paragraph of the introduction section). The Miyazaki, T. *et al.* teaching thus meets the limitations of claims 59 and 62. In addition, Miyazaki, T. *et al.* demonstrate that up-regulation of ZAKI-4 expression at transcriptional level (see abstract and Figures 2 and 3), indicating thyroid hormone receptor is an agonist for ZAKI-4 protein, as applied to claims 61 and 62. Miyazaki, T. *et al.* further demonstrate the expression pattern of ZAKI-4 in human muscle tissue (see Figure 6), as applied to the application claim 60.

Because the current application sets forth no sequence identifier in the claims and defines MCIP as muscle calcineurin interacting protein, and because ZAKI-4 is an analog of SEQ ID NO:3 (MCIP1), the Miyazaki, T. *et al.* reference anticipates claims 59-62 of the current application.

Please note that ZAKI-4 protein interacts with calcineurin and shows 62% sequence identity to SEQ ID NO:3 (MCIP1), and belongs to family of proteins containing a conserved motif of ISPPXSPP, which is assigned as DSCR1L1 by Human Nomenclature Committee.

Claims 59 and 61 are rejected under 35 U.S.C. 102 (a) as being anticipated by Fuentes, J. *et al.* (*Human Mol. Genet.* (July 1, 2000) 9, 1681-1690).

Fuentes *et al.* teaches that DSCR1 encoded protein (*i.e.,* MCP1), and that the DSCR1 transcript is expressed in human heart and skeletal muscles (see "Introduction" section) and the expression is stimulated by calcium and calcium biding protein, *i.e.*, calmodulin (see page 1687, the third paragraph and Figure 7 data), as applied to claim 59 and 61.

Claims 59-62 are rejected under 35 U.S.C. 102 (a) as being anticipated by Rothermel, B. *et al.* (*J. Biol. Chem.*, (March 24, 2000) 275, 8719-8725).

Rothermel *et al.* teach a process of regulating mammalian myoblast growth by MCIP1 protein which is up-regulated during muscle differentiation, and *co-expression* of the polypeptide, *i.e.*, calcineurin, in myocytes promotes expression of MCIP1 protein in cytoplasm (see Figure 6A, and the right column, page 8723), as applied to application claims 59, 61 and 62.

The current disclosure is also directed to a therapeutic method for treating muscle cells in a mammal that has a muscular cell associated disorder/disease by modulating MCIP expression. Accordingly, Rothermel *et al.* teach that the gene encoding MCIP1 is located on human chromosome 21 is a therapeutic target for cardiac-myocyte associated disorders (se the last paragraph, page 8725). The Rothermel teaching is applied to claims 60.

Therefore, the Rothermel *et al.* reference anticipates claims 59-62 of the current application.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483.

The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

SWL

January 20, 2003

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER